F ENT COOPERATION TREA .

From the INTERNATIONAL BUREAU

PCT

NOTIFICATION OF ELECTION

(PCT Rule 61.2)

To:

Assistant Commissioner for Patents
United States Patent and Trademark Office
Box PCT
Washington, D.C.20231
ETATS-UNIS D'AMERIQUE

in its capacity as elected Office

Date of mailing (day/month/year) 23 October 2000 (23.10.00)	
International application No. PCT/US00/05915	**Applicant's or agent's file reference** 11137/05002
International filing date (day/month/year) 08 March 2000 (08.03.00)	**Priority date** (day/month/year) 08 March 1999 (08.03.99)
Applicant STEELE, Christopher, L. et al	

1. The designated Office is hereby notified of its election made:

[X] in the demand filed with the International Preliminary Examining Authority on:

26 September 2000 (26.09.00)

[ ] in a notice effecting later election filed with the International Bureau on:

2. The election [X] was

[ ] was not

made before the expiration of 19 months from the priority date or, where Rule 32 applies, within the time limit under Rule 32.2(b).

The International Bureau of WIPO **34, chemin des Colombettes** **1211 Geneva 20, Switzerland**	Authorized officer Charlotte ENGER
Facsimile No.: (41-22) 740.14.35	Telephone No.: (41-22) 338.83.38

PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

14

Applicant's or agent's file reference	FOR FURTHER ACTION	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
11137/05002		

International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/US00/05915	08/03/2000	08/03/1999

International Patent Classification (IPC) or national classification and IPC
C12N15/53

Applicant
THE SAMUEL ROBERTS NOBLE FOUNDATION, INC. et al.

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 6 sheets, including this cover sheet.

   ☒ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

   These annexes consist of a total of 7 sheets.

3. This report contains indications relating to the following items:

   - I ☒ Basis of the report
   - II ☐ Priority
   - III ☐ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
   - IV ☐ Lack of unity of invention
   - V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations suporting such statement
   - VI ☒ Certain documents cited
   - VII ☐ Certain defects in the international application
   - VIII ☒ Certain observations on the international application

Date of submission of the demand	Date of completion of this report
26/09/2000	13.06.2001

Name and mailing address of the international preliminary examining authority:

European Patent Office
D-80298 Munich
Tel. +49 89 2399 - 0 Tx: 523656 epmu d
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Authorized officer

Huber, A

Telephone No. +49 89 2399 8173

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/US00/05915

I. Basis of the report

1. With regard to the **elements** of the international application *(Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17))*:
Description, pages:

1-28	as originally filed				

Claims, No.:

1-65	as received on	14/05/2001	with letter of	01/05/2001	

Drawings, sheets:

1/15-15/15	as originally filed				

Sequence listing part of the description, pages:

1-11, filed with the letter of 21.06.2000

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

   These elements were available or furnished to this Authority in the following language: , which is:

   - ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).
   - ☐ the language of publication of the international application (under Rule 48.3(b)).
   - ☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

   - ☐ contained in the international application in written form.
   - ☐ filed together with the international application in computer readable form.
   - ☒ furnished subsequently to this Authority in written form.
   - ☒ furnished subsequently to this Authority in computer readable form.
   - ☒ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
   - ☒ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

- ☐ the description, pages:
- ☐ the claims, Nos.:
- ☐ the drawings, sheets:

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)):

   (Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)

6. Additional observations, if necessary:

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	1-65
	No:	Claims	
Inventive step (IS)	Yes:	Claims	1-65
	No:	Claims	
Industrial applicability (IA)	Yes:	Claims	1-65
	No:	Claims	

2. Citations and explanations
   see separate sheet

VI. Certain documents cited

1. Certain published documents (Rule 70.10)

and / or

2. Non-written disclosures (Rule 70.9)

   see separate sheet

VIII. Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:
see separate sheet

Re Item V

Reasoned statement under Article 35(2) with regard to novelty, inventive st p or industrial applicability; citations and explanations supporting such statem nt

1. The present application relates to the isolation of genes catalysing the first step of the isoflavone synthase reaction (CYP93C) and the introduction of these genes into plant cells.

2. Reference is made to the following document:

   D1: SIMINSZKY B. ET AL.: 'Cytochrome P450 monooxygenase CYP93C1p from soybean; AC AF022462' EBI DATABASE, 8 January 1998 (1998-01-08), XP002143672 cited in the application & SIMINSZKY B. ET AL.: 'Expression of a soybean cytochrome P450 monooxygenase cDNA in yeast and tobacco enhances the metabolism of phenylurea herbicides' PNAS,U.S.A., vol. 96, February 1999 (1999-02), pages 1750-1755, XP002100400

3. Novelty and inventive step (Art.33(2) and (3) PCT):

3.1 D1 discloses the nucleotide sequence of the cytochrome P450 monooxygenase CYP93C1. The sequence is almost identical to the sequence shown in SEQ ID No. 1 of present application (>98% identity in a 1659 bp overlap) and, except for three nucleotide differences it is identical in the portion consisting of nucleotide 36 to nucleotide 1598 of SEQ ID No. 1.

3.2 Amended Claim 34 requires that the portion which encodes a cytochrome P450 of the CYP93 family **consists** of nucleotides 36 to 1598 of SEQ ID No. 1. Due to the differences in the coding sequence of CYP93C1p (D1) and CYP93C1v2 (SEQ ID No.1 of present application), novelty of Claims 34-37 is acknowledged.

Since the function of the cytochrome P450 CYP93C1 of D1 was unknown, the skilled person would have no motivation to start from D1 in the attempt to find a variant of the gene disclosed in D1. Therefore, also an inventive step is recognized for the subject-matter of Claims 34-37.

3.3 Also the subject-matter of the other claims is considered to be novel and inventive. An enzyme which catalyzes the first step of the isoflavone synthase reaction has not been available from the prior art and does not seem to be directly and unambiguously derivable from any of the cited documents. The function of the gene product encoded by CYP93C1 (D1) was unknown and the gene has not been used for transforming plants. The skilled person would therefore not be prompted to use the sequence disclosed in D1 to produce transgenic plants which produce isoflavones and to use said plants according to the present invention.

R Item VI

Certain documents cited

Application No Patent No	Publication date *(day/month/year)*	Filing date *(day/month/year)*	Priority date *(valid claim)* *(day/month/year)*
WO-A-99/19493	22.04.99	05.10.98	10.10.97

Said document has been published after but filed before the claimed priority date of present application. It does therefore not constitute prior art in the sense of Rule 64(1)(b) PCT. It may, however, become of relevance for the novelty of the claimed subject-matter during regional phase examination and, if it later turns out that the priority of the present application has not been correctly claimed, also for the inventive step involved with the claimed subject-matter.

Re Item VIII

Certain observations on the international application

1. Claim 1 does not meet the requirements of Article 6 PCT in that the matter for which protection is sought is not clearly defined. An enzyme which is capable of catalysing the aryl migration of a flavanone to form an isoflavanone intermediate

(isoflavanone synthase) has apparently not been available in the prior art.
The claim therefore attempts to define the subject-matter in terms of the result to be achieved which merely amounts to a statement of the underlying problem.
The technical features necessary for achieving this result should be added. In the present case the DNA segment encoding the enzyme has to be defined by those technical features which allow the skilled person to clearly identify the matter for which protection is sought (e.g. the nucleotide sequence of the gene encoding the enzyme).
The same remark applies mutatis mutandis to all independent claims wherein the DNA segment encoding the isoflavanone synthase is defined as in Claim 1.

2. The term "CYP93C" gene which is used in the claims to define the DNA segment encoding the isoflavanone synthase is an internal designation which does not provide any technical teaching to the reader. A chemical compound such as a gene has to be defined by true technical features which allow the unambiguous identification of the claimed matter, e.g. in terms of the nucleotide sequence.
The applicant argues that the designation CYP93C is an accepted term which refers to a subfamily of the ninety-third family of P450 enzymes. It may be accepted that members of the CYP93 family have been known in the prior art (see e.g. Akashi et al., FEBS Letters 432 (1998), pp. 287-290) where cDNA encoding CYP93B1, which encodes an enzyme with F2H activity is described). However, a P450 enzyme encoding isoflavanone synthase was apparently not known from the prior art. Therefore, definition of the enzyme by a family name is of no help for the identification of the respective enzyme. In addition, the post-published patent application WO 99/19493 mentions on page 27, l. 18-20, that CYP93C1 defined a new subfamily.
Consequently, claims in which the gene encoding isoflavanone synthase is merely defined by reference to the term CYP93C are unclear and do not meet the requirements of Art. 6 PCT.

3. Claim 52 is directed to a method of transforming a plant. However, no method steps are indicated in the claim.

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.TENT COOPERATION TREAT

PCT

INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference	**FOR FURTHER ACTION**	see Notification of Transmittal of International Search Report (Form PCT/ISA/220) as well as, where applicable, item 5 below.
11137/05002		
International application No.	International filing date *(day/month/year)*	(Earliest) Priority Date *(day/month/year)*
PCT/US 00/ 05915	08/03/2000	08/03/1999
Applicant		
THE SAMUEL ROBERTS NOBLE FOUNDATION, INC. et al.		

This International Search Report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This International Search Report consists of a total of 5 sheets.

[X] It is also accompanied by a copy of each prior art document cited in this report.

1. **Basis of the report**

   a. With regard to the **language,** the international search was carried out on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

   [ ] the international search was carried out on the basis of a translation of the international application furnished to this Authority (Rule 23.1(b)).

   b. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international search was carried out on the basis of the sequence listing :

   [X] contained in the international application in written form.

   [ ] filed together with the international application in computer readable form.

   [ ] furnished subsequently to this Authority in written form.

   [X] furnished subsequently to this Authority in computer readble form.

   [X] the statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

   [X] the statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished

2. [X] **Certain claims were found unsearchable** (See Box I).

3. [ ] **Unity of invention is lacking** (see Box II).

4. With regard to the **title,**

   [X] the text is approved as submitted by the applicant.

   [ ] the text has been established by this Authority to read as follows:

5. With regard to the **abstract,**

   [X] the text is approved as submitted by the applicant.

   [ ] the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box III. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.

6. The figure of the **drawings** to be published with the abstract is Figure No. 1

   [X] as suggested by the applicant.

   [ ] because the applicant failed to suggest a figure.

   [ ] because this figure better characterizes the invention.

   [ ] None of the figures.

INTERNATIONAL SEARCH REPORT

[redacted]tional Application No
PCT/US 00/05915

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 C12N15/53 C12N15/82 C12N15/11 C12N9/02 C12N5/10
A01H5/00 A01H5/10 A23L1/00

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 7 C12N A01H A23L

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)
EPO-Internal, BIOSIS

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	SIMINSZKY B. ET AL.: "Cytochrome P450 monooxygenase CYP93C1p from soybean; AC AF022462" EBI DATABASE, 8 January 1998 (1998-01-08), XP002143672 cited in the application the whole document & SIMINSZKY B. ET AL.: "Expression of a soybean cytochrome P450 monooxygenase cDNA in yeast and tobacco enhances the metabolism of phenylurea herbicides" PNAS,U.S.A., vol. 96, February 1999 (1999-02), pages 1750-1755, XP002100400 the whole document --- -/--	74-77

[X] Further documents are listed in the continuation of box C.

[X] Patent family members are listed in annex.

° Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
27 July 2000	10/08/2000

Name and mailing address of the ISA	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL – 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	Kania, T

1

Form PCT/ISA/210 (second sheet) (July 1992)

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	COLLIVER S P ET AL: "Differential modification of flavonoid and isoflavonoid biosynthesis with an antisense chalcone synthase construct in transgenic Lotus corniculatus." PLANT MOLECULAR BIOLOGY, vol. 35, no. 4, 1997, pages 509-522, XP002143673 ISSN: 0167-4412 the whole document	1-104
A	PAIVA N L ET AL: "REGULATION OF ISOFLAVONOID METABOLISM IN ALFALFA" PLANT CELL, TISSUE AND ORGAN CULTURE,XX,KLUWER ACADEMIC PUBLISHERS, vol. 38, no. 2/03, 1994, pages 213-220, XP000571330 ISSN: 0167-6857 the whole document	1-104
A	OTANI K. ET AL.: "Licodione synthase, a cytochrome P-450 monooxygenase catalyzing 2-Hydroxylation of 5-Deoxyflavanone in cultured Glycyrrhiza achinata L. cells" PLANT PHYSIOLOGY, vol. 105, 1994, pages 1427-1432, XP002143674 the whole document	1-104
A	AKASHI T. ET AL.: "Identification of a cytochrome P450 cDNA encoding (2S)-flavanone 2-hydroxylase of licorice (Glycyrrhiza echinata L.; Fabaceae) which represents licodione synthase and flavone synthase" FEBS LETTERS, vol. 431, 1998, pages 287-290, XP002927621 cited in the application the whole document	1-104
A	WO 96 15239 A (SAMUEL ROBERTS NOBLE FOUNDATIO) 23 May 1996 (1996-05-23) the whole document	1-104
A	DIXON RICHARD A ET AL: "The isoflavonoid phytoalexin pathway: From enzymes to genes to transcription factors." PHYSIOLOGIA PLANTARUM, vol. 93, no. 2, 1995, pages 385-392, XP000925614 ISSN: 0031-9317 the whole document	1-104

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1

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication,where appropriate, of the relevant passages	Relevant to claim No.
A	DIXON, R. A. ET AL: "Molecular controls for isoflavonoid biosynthesis in relation to plant and human health" 1999 , PHYTOCHEMICALS IN HUMAN HEALTH PROTECTION, NUTRITION, AND PLANT DEFENSE, (1999) PP. 133-159. 99 REF. PUBLISHER: KLUWER ACADEMIC/PLENUM PUBLISHERS. NEW YORK ISBN: 0-306-46203-6 XP000925618 see esp. pp.143/44 ---	1-104
P,X	AKASHI TOMOYOSHI ET AL: "Cloning and functional expression of a cytochrome P450 cDNA encoding 2-hydroxyisoflavanone synthase involved in biosynthesis of the isoflavonoid skeleton in licorice." PLANT PHYSIOLOGY (ROCKVILLE), vol. 121, no. 3, November 1999 (1999-11), pages 821-828, XP002143675 ISSN: 0032-0889 see esp. p.1431 r.col. the whole document ---	41
P,X	WO 99 19493 A (UNIV NORTH CAROLINA ;DEWEY RALPH E (US); CORBIN FREDERICK T (US);) 22 April 1999 (1999-04-22) see esp. example 2; SEQ ID NO:9 ---	74-77
P,X	STEELE CHRISTOPHER L ET AL: "Molecular characterization of the enzyme catalyzing the aryl migration reaction of isoflavonoid biosynthesis in soybean." ARCHIVES OF BIOCHEMISTRY AND BIOPHYSICS, vol. 367, no. 1, 1 July 1999 (1999-07-01), pages 146-150, XP000925681 ISSN: 0003-9861 the whole document ---	74-77
P,X	JUNG WOOSUK ET AL: "Identification and expression of isoflavone synthase, the key enzyme for biosynthesis of isoflavones in legumes." NATURE BIOTECHNOLOGY, vol. 18, no. 2, February 2000 (2000-02), pages 208-212, XP002143676 ISSN: 1087-0156 the whole document -----	1-5, 8-10,15, 16,20, 21, 47-51, 54-56, 74-77, 89, 99-102

1

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No
PCT/US 00/05915

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 9615239 A	23-05-1996	US 5750399 A	12-05-1998
		AU 699496 B	03-12-1998
		AU 3972795 A	06-06-1996
		CA 2204131 A	23-05-1996
		EP 0792356 A	03-09-1997
		JP 10508750 T	02-09-1998
		NZ 296033 A	25-02-1999
WO 9919493 A	22-04-1999	AU 9680698 A	03-05-1999

WE CLAIM:

1. A method for introducing into a naturally non-isoflavonoid-producing plant species the enzyme catalyzing the aryl migration of a flavanone to form an isoflavanone intermediate or an isoflavone, comprising:

introducing a DNA segment encoding said enzyme into said plant to form a transgenic plant, wherein said transgenic plant expresses said DNA segment under the control of a suitable constitutive or inducible promoter when said transgenic plant is exposed to conditions which permit expression.

2. The method of Claim 1, wherein said DNA segment comprises isolated genomic DNA.

3. The method of Claim 1, wherein said DNA segment comprises recombinant DNA.

4. The method of Claim 1, 2 or 3, wherein said DNA segment comprises a CYP93C gene.

5. The method of Claim 4, wherein said DNA segment consists essentially of the sequence from about nucleotide 36 to about nucleotide 1598 of the sequence depicted in SEQ ID NO:1.

6. The method of Claim 1, 2 or 3, wherein said DNA segment comprises a *Medicago truncatula* homolog of a CYP93C gene.

7. The method of Claim 6, wherein said DNA segment consists essentially of the sequence from about nucleotide 92 to about nucleotide 1657 of the sequence depicted in SEQ ID NO:4.

8. The method of Claim 1, wherein chalcone synthase, chalcone reductase, and chalcone isomerase genes are also expressed in said plant to cause in vivo formation of daidzein or a daidzein derivative.

9. The method of Claim 2, wherein chalcone synthase, chalcone reductase, and chalcone isomerase genes are also expressed in said plant to cause in vivo formation of daidzein or a daidzein derivative.

10. The method of Claim 3, wherein chalcone synthase, chalcone reductase, and chalcone isomerase genes are also expressed in said plant to cause in vivo formation of daidzein or a daidzein derivative.

11. The method of Claim 8, 9 or 10, wherein said plant is further transformed to comprise said chalcone synthase, chalcone reductase, and chalcone isomerase genes.

12. The method of Claim 1, 2, 3, 8, 9 or 10, wherein said plant further comprises downstream genes to metabolize said formed isoflavanone intermediate or isoflavone to biologically active isoflavonoid derivatives or conjugates.

13. The method of Claim 12, wherein said downstream gene is selected from the group consisting of isoflavone *O*-methyltransferase, isoflavone 2'-hydroxylase, isoflavone reductase, and vestitone reductase.

14. The method of Claim 13, wherein said plant comprises downstream gene 4'-*O*-methyltransferase to form biochanin A or a biochanin A derivative.

15. The method of Claim 1, 2, 3, 5, 7, 8, 9, 10, 13 or 14, wherein said flavanone is liquiritigenin.

16. The method of Claim 4, wherein said flavanone is liquiritigenin.

17. The method of Claim 6, wherein said flavanone is liquiritigenin.

18. The method of Claim 11, wherein said flavanone is liquiritigenin.

19. The method of Claim 12, wherein said flavanone is liquiritigenin.

20. The method of Claim 1, 2, 3, 5, 7, 8, 9, 10, 13 or 14, wherein said flavanone is naringenin.

21. The method of Claim 4, wherein said flavanone is naringenin.

22. The method of Claim 6, wherein said flavanone is naringenin.

23. The method of Claim 11, wherein said flavanone is naringenin.

24. The method of Claim 12, wherein said flavanone is naringenin.

25. A method for increasing the level of isoflavonoid compounds in naturally isoflavonoid-producing plants comprising:

introducing a DNA segment encoding the enzyme catalyzing the aryl migration of a flavanone to yield an isoflavonoid to form a transgenic plant, wherein said transgenic plant expresses said DNA segment under the control of a suitable constitutive or inducible promoter when said transgenic plant is exposed to conditions which permit expression.

26. The method of Claim 25, wherein said isoflavonoid is selected from the group consisting of an isoflavanone intermediate, an isoflavone, an isoflavone derivative, and an isoflavone conjugate.

27. The method of Claim 25, wherein said DNA segment comprises isolated genomic DNA.

28. The method of Claim 26, wherein said DNA segment comprises isolated genomic DNA.

29. The method of Claim 25, wherein said DNA segment comprises recombinant DNA.

30. The method of Claim 26, wherein said DNA segment comprises recombinant DNA.

31. The method of Claim 25, 26, 27, 28, 29 or 30, wherein said DNA segment comprises a CYP93C gene.

32. The method of Claim 31, wherein said DNA segment consists essentially of the sequence from about nucleotide 36 to about nucleotide 1598 of the sequence depicted in SEQ ID NO:1.

33. The method of Claim 25, 26, 27, 28, 29 or 30, wherein said DNA segment is a *Medicago truncatula* homolog of a CYP93C gene.

34. The method of Claim 33, wherein said DNA segment consists essentially of the sequence from about nucleotide 92 to about nucleotide 1657 of the sequence depicted in SEQ ID NO:4.

35. The method of Claim 25, 26, 27, 28, 29, 30, 32 or 34, wherein said flavanone is liquiritigenin.

36. The method of Claim 31, wherein said flavanone is liquiritigenin.

37. The method of Claim 33, wherein said flavanone is liquiritigenin.

38. The method of Claim 25, 26, 27, 28, 29, 30, 32 or 34, wherein said flavanone is naringenin.

39. The method of Claim 31, wherein said flavanone is naringenin.

40. The method of Claim 33, wherein said flavanone is naringenin.

41. A method for synthesizing an isoflavanone intermediate or an isoflavone from a flavanone by expressing a recombinant CYP93C gene segment in a suitable bacterial, fungal, algal, or insect cell system.

42. The method of Claim 41, wherein said gene segment consists essentially of the sequence from about nucleotide 36 to about nucleotide 1598 of the sequence depicted in SEQ ID NO:1.

43. The method of Claim 41, wherein said gene segment consists essentially of the sequence from about nucleotide 92 to about nucleotide 1657 of the sequence depicted in SEQ ID NO:4.

44. A method of reducing the levels of isoflavonoid compounds in a naturally isoflavonoid-producing plant comprising introducing and expressing an antisense or gene silencing construct that contains an intact CYP93C gene or segments thereof into said plant.

45. The method of Claim 44, wherein said gene consists essentially of the sequence from about nucleotide 36 to about nucleotide 1598 of the sequence depicted in SEQ ID NO:1.

46. The method of Claim 44, wherein said gene consists essentially of the sequence from about nucleotide 92 to about nucleotide 1657 of the sequence depicted in SEQ ID NO:4.

47. A naturally non-isoflavonoid-producing plant cell transformed by introducing a DNA segment encoding the enzyme catalyzing the aryl migration of a flavanone to form an isoflavanone intermediate or an isoflavone, wherein said transgenic plant cell expresses said DNA segment under the control of a suitable constitutive or inducible promoter when exposed to conditions which permit expression.

48. The plant cell of Claim 47, wherein said DNA segment comprises isolated genomic DNA.

49. The plant cell of Claim 47, wherein said DNA segment comprises recombinant DNA.

50. The plant cell of Claim 47, 48 or 49, wherein said DNA segment comprises a CYP93C gene.

51. The plant cell of Claim 50, wherein said DNA segment consists essentially of the sequence from about nucleotide 36 to about nucleotide 1598 of the sequence depicted in SEQ ID NO:1.

52. The plant cell of Claim 47, 48 or 49, wherein said DNA segment comprises a *Medicago truncatula* homolog of a CYP93C gene.

53. The plant cell of Claim 52, wherein said DNA segment consists essentially of the sequence from about nucleotide 92 to about nucleotide 1657 of the sequence depicted in SEQ ID NO:4.

54. The plant cell of Claim 47, wherein chalcone synthase, chalcone reductase, and chalcone isomerase genes are also expressed in said plant cell to cause in vivo formation of daidzein or a daidzein derivative.

55. The plant cell of Claim 48, wherein chalcone synthase, chalcone reductase, and chalcone isomerase genes are also expressed in said plant cell to cause in vivo formation of daidzein or a daidzein derivative.

56. The plant cell of Claim 49, wherein chalcone synthase, chalcone reductase, and chalcone isomerase genes are also expressed in said plant cell to cause in vivo formation of daidzein or a daidzein derivative.

57. The plant cell of Claim 54, 55 or 56, wherein said plant cell is further transformed to comprise said chalcone synthase, chalcone reductase, and chalcone isomerase genes.

58. The plant cell of Claim 47, 48, 49, 54, 55 or 56, wherein said plant cell further comprises downstream genes to metabolize said formed isoflavanone intermediate or isoflavone to biologically active isoflavonoid derivatives or conjugates.

59. The plant cell of Claim 58, wherein said downstream gene is selected from the group consisting of isoflavone *O*-methyltransferase, isoflavone 2'-hydroxylase, isoflavone reductase, and vestitone reductase.

60. The plant cell of Claim 59, wherein said plant cell comprises downstream gene 4'-*O*-methyltransferase to cause in vivo formation of biochanin A or a biochanin A derivative.

61. A naturally isoflavonoid-producing plant cell transformed by introducing a DNA segment encoding the enzyme catalyzing the aryl migration of a flavanone to yield an isoflavonoid to form a transformed plant cell, wherein said transformed plant cell expresses said DNA segment under the control of a suitable constitutive or inducible promoter when exposed to conditions which permit expression.

62. The plant cell of Claim 61, wherein said isoflavonoid is selected from the group consisting of an isoflavanone intermediate, an isoflavone, an isoflavone derivative, and an isoflavone conjugate.

63. The plant cell of Claim 61, wherein said DNA segment comprises isolated genomic DNA.

64. The plant cell of Claim 62, wherein said DNA segment comprises isolated genomic DNA.

65. The plant cell of Claim 61, wherein said DNA segment comprises recombinant DNA.

66. The plant cell of Claim 62, wherein said DNA segment comprises recombinant DNA.

67. The plant cell of Claim 61, 62, 63, 64, 65 or 66, wherein said DNA segment comprises a CYP93C gene.

68. The plant cell of Claim 67, wherein said DNA segment consists essentially of the sequence from about nucleotide 36 to about nucleotide 1598 of the sequence depicted in SEQ ID NO:1.

69. The plant cell of Claim 61, 62, 63, 64, 65 or 66, wherein said DNA segment is a *Medicago truncatula* homolog of a CYP93C gene.

70. The plant cell of Claim 69, wherein said DNA segment consists essentially of the sequence from about nucleotide 92 to about nucleotide 1657 of the sequence depicted in SEQ ID NO:4.

71. A transgenic plant cell having reduced levels of isoflavonoid compounds, said plant cell transformed by introducing an antisense or gene silencing construct that contains an intact CYP93C gene or segments thereof into said plant cell.

72. The plant cell of Claim 71, wherein said gene consists essentially of the sequence from about nucleotide 36 to about nucleotide 1598 of the sequence depicted in SEQ ID NO:1.

73. The plant cell of Claim 71, wherein said gene consists essentially of the sequence from about nucleotide 92 to about nucleotide 1657 of the sequence depicted in SEQ ID NO:4.

74. An isolated gene or DNA segment comprising a portion which encodes a cytochrome P450 of the CYP93 family that can catalyze the aryl migration of a flavanone to yield an isoflavanone intermediate or an isoflavone, wherein said portion consists essentially of about nucleotide 36 to about nucleotide 1598 of the sequence depicted in SEQ ID NO:1.

75. The gene or DNA segment of Claim 74, wherein said gene is the soybean gene encoding the enzyme catalyzing the aryl migration of liquiritigenin.

76. The gene or DNA segment of Claim 74, wherein said gene is the soybean gene encoding the enzyme catalyzing the aryl migration of naringenin.

77. A protein encoded by a portion of an isolated gene or DNA segment which encodes a cytochrome P450 that can catalyze the aryl migration of a flavanone to yield an isoflavanone intermediate or an isoflavone, wherein said portion consists essentially of about nucleotide 36 to about nucleotide 1598 of the sequence depicted in SEQ ID NO:1.

78. An isolated gene or DNA segment comprising a portion which encodes a cytochrome P450 that can catalyze the aryl migration of a flavanone to yield an isoflavanone intermediate or an isoflavone, wherein said portion is a *Medicago truncatula* homolog of a CYP93C gene.

79. The gene or DNA segment of Claim 78 consisting essentially of about nucleotide 92 to about nucleotide 1657 of the sequence depicted in SEQ ID NO:4

80. The gene or DNA segment of Claim 78, wherein said gene is the *Medicago truncatula* gene encoding the enzyme catalyzing the aryl migration of liquiritigenin.

81. The gene or DNA segment of Claim 79, wherein said gene is the *Medicago truncatula* gene encoding the enzyme catalyzing the aryl migration of liquiritigenin.

82. The gene or DNA segment of Claim 78, wherein said gene is the *Medicago truncatula* gene encoding the enzyme catalyzing the aryl migration of naringenin.

83. The gene or DNA segment of Claim 79, wherein said gene is the *Medicago truncatula* gene encoding the enzyme catalyzing the aryl migration of naringenin.

84. A protein encoded by a portion of an isolated gene or DNA segment which encodes a cytochrome P450 that can catalyze the aryl migration of a flavanone to yield an isoflavanone intermediate or an isoflavone, wherein said portion is a *Medicago truncatula* homolog of a CYP93C gene.

85. A food comprising edible transgenic plant material capable of being ingested for its nutritional value, said transgenic plant is transformed with an isolated gene or DNA segment which encodes a cytochrome P450 that can catalyze the aryl migration of a flavanone to yield an isoflavanone intermediate or an isoflavone, wherein said transgenic plant exhibits increased levels of an isoflavonoid when compared to the level of said isoflavonoid in plants of the same species which do not comprise said isolated gene or DNA segment.

86. A food comprising at least one isoflavonoid, wherein said isoflavonoid is isolated from a transgenic plant transformed with an isolated gene or DNA segment

which encodes a cytochrome P450 that can catalyze the aryl migration of a flavanone to yield an isoflavanone intermediate or an isoflavone, wherein said transgenic plant exhibits increased levels of an isoflavonoid when compared to the level of said isoflavonoid in plants of the same species which do not comprise said isolated gene or DNA segment.

87. A composition comprising at least a portion of a transgenic plant transformed with an isolated gene or DNA segment which encodes a cytochrome P450 that can catalyze the aryl migration of a flavanone to yield an isoflavanone intermediate or an isoflavone, wherein said transgenic plant exhibits increased levels of an isoflavonoid when compared to the level of said isoflavonoid in plants of the same species which do not comprise said isolated gene or DNA segment, said composition suitable for ingestion as a food stuff, a nutritional supplement, an animal feed supplement, or a nutraceutical.

88. A composition comprising an isoflavonoid suitable for administration as a food stuff, a nutritional supplement, an animal feed supplement, a nutraceutical, or a pharmaceutical, said isoflavonoid isolated from at least a portion of a transgenic plant transformed with an isolated gene or DNA segment which encodes a cytochrome P450 that can catalyze the aryl migration of a flavanone to yield an isoflavanone intermediate or an isoflavone, wherein said transgenic plant exhibits increased levels of an isoflavonoid when compared to the level of said isoflavonoid in plants of the same species which do not comprise said isolated gene or DNA segment.

89. A method of increasing the nutritional value of a plant by transforming said plant with an isolated gene or DNA segment which encodes a cytochrome P450 that can catalyze the aryl migration of a flavanone to yield an isoflavanone intermediate or an isoflavone, wherein said transgenic plant exhibits increased levels of an isoflavonoid when compared to the level of said isoflavonoid in plants of the same species which do not comprise said isolated gene or DNA segment.

90. A method of using a transgenic plant transformed with an isolated gene or DNA segment which encodes a cytochrome P450 that can catalyze the aryl migration of a flavanone to yield an isoflavanone intermediate or an isoflavone, wherein said transgenic plant exhibits an increased level of an isoflavonoid when compared to the level of said isoflavonoid in plants of the same species which do not comprise said isolated gene or DNA segment, to provide a nutraceutical benefit to a human or animal administered said isoflavonoid.

91. The method of claim 90, wherein said isoflavonoid is administered by ingestion of at least a portion of said plant.

92. The method of claim 90, wherein said isoflavonoid is administered by ingestion of a composition comprising an isoflavonoid isolated from said plant.

93. A method of using an isoflavonoid isolated from a transgenic plant transformed with an isolated gene or DNA segment which encodes a cytochrome P450 that can catalyze the aryl migration of a flavanone to yield an isoflavanone intermediate or an isoflavone, wherein said transgenic plant exhibits an increased level of an isoflavonoid when compared to the level of said isoflavonoid in plants of the same species which do not comprise said isolated gene or DNA segment, to provide a pharmaceutical benefit to a patient administered said isoflavonoid.

94. A method of increasing disease resistance in a plant by transforming said plant with an isolated gene or DNA segment which encodes a cytochrome P450 that can catalyze the aryl migration of a flavanone to yield an isoflavanone intermediate or an isoflavone, wherein said transgenic plant exhibits an increased level of an isoflavonoid when compared to the level of said isoflavonoid in plants of the same species which do not comprise said isolated gene or DNA segment.

95. A method of increasing nodulation efficiency of a leguminous plant by transforming said plant with an isolated gene or DNA segment which encodes a cytochrome P450 that can catalyze the aryl migration of a flavanone to yield an isoflavanone intermediate or an isoflavone, wherein said transgenic plant exhibits an increased level of an isoflavonoid released from the roots of said transgenic plant when compared to the level of the isoflavonoid released from the roots of plants of the same species which do not comprise said isolated gene or DNA segment.

96. A leguminous transgenic plant exhibiting increased nodulation efficiency, wherein said transgenic plant is transformed with an isolated gene or DNA segment which encodes a cytochrome P450 that can catalyze the aryl migration of a flavanone to yield an isoflavanone intermediate or an isoflavone, and wherein said transgenic plant exhibits an increased level of an isoflavonoid released from the roots of said transgenic plant when compared to the level of the isoflavonoid released from the roots of plants of the same species which do not comprise said isolated gene or DNA segment.

97. A method of increasing bacterial or fungal symbiosis in a plant by transforming said plant with an isolated gene or DNA segment which encodes a cytochrome P450 that can catalyze the aryl migration of a flavanone to yield an isoflavanone intermediate or an isoflavone, wherein said transgenic plant exhibits an increased level of an isoflavonoid when compared to the level of said isoflavonoid in plants of the same species which do not comprise said isolated gene or DNA segment.

98. A transgenic plant exhibiting an increased level of bacterial or fungal symbiosis, wherein said transgenic plant is transformed with an isolated gene or DNA segment which encodes a cytochrome P450 that can catalyze the aryl migration of a flavanone to yield an isoflavanone intermediate or an isoflavone, and wherein said transgenic plant exhibits an increased level of an isoflavonoid when compared to the level of said isoflavonoid in plants of the same species which do not comprise the isolated gene or DNA segment.

99. A transgenic plant comprising at least one recombinant DNA sequence encoding a cytochrome P450 that can catalyze the aryl migration of a flavanone to yield an isoflavanone intermediate or an isoflavone, wherein said transgenic plant exhibits an increased level of an isoflavonoid when compared to the level of said isoflavonoid in plants of the same species which do not comprise said recombinant DNA sequence.

100. Seed from a transgenic plant comprising at least one recombinant DNA sequence encoding a cytochrome P450 that can catalyze the aryl migration of a flavanone to yield an isoflavanone intermediate or an isoflavone, wherein said transgenic plant exhibits an increased level of an isoflavonoid when compared to the level of said isoflavonoid in plants of the same species which do not comprise said recombinant DNA sequence.

101. Progeny from a transgenic plant comprising at least one recombinant DNA sequence encoding a cytochrome P450 that can catalyze the aryl migration of a flavanone to yield an isoflavanone intermediate or an isoflavone, wherein said transgenic plant exhibits an increased level of an isoflavonoid when compared to the level of said isoflavonoid in plants of the same species which do not comprise said recombinant DNA sequence.

102. Progeny from seed of a transgenic plant comprising at least one recombinant DNA sequence encoding a cytochrome P450 that can catalyze the aryl migration of a flavanone to yield an isoflavanone intermediate or an isoflavone, wherein said transgenic plant exhibits an increased level of an isoflavonoid when compared to the level of said isoflavonoid in plants of the same species which do not comprise said recombinant DNA sequence.

103. Use of a transgenic plant transformed with an isolated gene or DNA segment which encodes a cytochrome P450 that can catalyze the aryl migration of a flavanone to yield an isoflavanone intermediate or an isoflavone, wherein said transgenic plant exhibits an increased level of an isoflavonoid when compared to the level of said isoflavonoid in plants of the same species which do not comprise said

isolated gene or DNA segment, for the preparation of a nutraceutical preparation for achieving a nutritional effect.

104. Use of a transgenic plant transformed with an isolated gene or DNA segment which encodes a cytochrome P450 that can catalyze the aryl migration of a flavanone to yield an isoflavanone intermediate or an isoflavone, wherein said transgenic plant exhibits an increased level of an isoflavonoid when compared to the level of said isoflavonoid in plants of the same species which do not comprise said isolated gene or DNA segment, for the preparation of a pharmaceutical preparation for achieving a therapeutic effect.